



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460**

MAR 22 2007

OFFICE OF PESTICIDES AND TOXIC

MEMORANDUM

SUBJECT: Science Review of efficacy studies (MRIDs 470191-01, 470191-02, 470191-03, and 470191-04) of Conceal Candle, EPA Reg. No. 70909-5, containing 3.50 % linalool (PC Code: 128838) as its active ingredient.

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Decision No. 371138
Barcode DP: 336294
PC Code: 128838
CAS: 78-70-6
File No. 70909-5
MRIDs 470191-01, 470191-02, 470191-03, and 470191-04

ACTION REQUESTED

BioSensory Inc. submitted conditionally required efficacy studies designed to evaluate efficacy of Conceal Candles (EPA No 70909- 5), containing 3.50 % linalool (PC Code: 128838) as its active ingredient, to repel mosquitoes.

MRID 470191-01 *Release Rate of Linolool from Conceal Candles in Storage Conditions*

MRID 470191-02 *Linalool Candles as Spatial Repellents Against Natural Populations of Mosquitoes in Anahuac National Wildlife Refuge, Anahuac, Texas*

MRID 470191-03 *Candles as Spatial Repellents Against Natural Populations of Mosquitoes in Arthur R. Marshall Loxahatchee National Wildlife Refuge, Boynton Beach, Florida.*

MRID 470191-04 *Field Evaluation of One Year Old 3.5% Linalool Candles Against Mosquitoes in Connecticut, USA.*

CONCLUSIONS AND RECOMMENDATIONS.

A. The currently submitted studies, MRIDs 470191-01 and 470191-02, and 470191-03 adequately address the following deficiencies:

1. Release rate of linalool from unlit candles in a warehouse environment.
2. Assessment of biting pressure conducted at time of the study.
3. Proper negative control requiring that one of the treatments is without Conceal candle.
4. Verification that the test material is the product proposed for registration, containing a concentration of 3.5 % w/w linalool
5. The submitted studies address OPPTS 810.3700 *Insect Repellents for Human Skin and Outdoor Premises*, which recommends at least 2 field tests in 2 different habitats, containing different species, within the same state or geographical region.

B. The registrant needs to address the following deficiencies concerning efficacy results:

1. Calculated and the reported values of percent reduction in landings are inconsistent.
 - a) Calculations from reported data in MIRD 470191-03 show a lower level of efficacy than reported. The investigator concludes that mosquito landings were reduced by an average of 67% compared to control in test A, 68 % in test B, and 58 % in test C at a confidence level of 99%. The study report does not explain how these percentages were calculated. The reported percentages do not coincide with percent reduction in number of mosquitoes relative to control when the number of mosquitoes collected at control stations are subtracted from the number of mosquitoes collected at the treatment stations, and this difference is divided by the corresponding number of mosquitoes collected at the control station. The percentages calculated as described above show mean reductions of 48, 56, and 40 percent for test stations A, B, and C, respectively. These percentage reductions are lower than the ones reported.

- b) Calculations from reported data in MIRD 470191-02 show a lower level of efficacy than reported. The investigator concludes that the reduction in mosquito landings due to the presence of the candle was 80% relative to control. The difference between control and treatment captured mosquitoes divided by the total number of mosquitoes captured at the corresponding control station shows 60 % mean reduction in number of mosquitoes due to the presence of the candle. This calculated mean percent reduction in mosquito landings relative to control is lower than that reported for efficacy of linalool candles.
 - c) The registrant needs to clarify how the reported percentages were calculated in order to verify the reported results.
2. The dates reported in the MRID 470191-03 are inconsistent. Figures 1, 2, and 3 show that the data was collected in 2006. However, the report specifies that the study was conducted in March, 2004, and the data was analyzed in 2006. The graphs legend must indicate the date when the data was collected.
 3. Study MRID 470191-04, *Field Evaluation of One Year Old 3.5% Linalool Candles Against Mosquitoes in Connecticut, USA*, is inconclusive due to lack of information. The study report only includes a graph which shows that the total mosquitoes collected are below the >5 human landing rate counts stated on page 4.

NOTE TO RAL: *These studies involve the use of human subjects. If at least one of these studies was conducted after April 7, 2006, the registrant needs to submit the documentation required for reviewing the ethical performance of the study.*

C. Label Review

1. On product label Directions for Use, recommended number of candles, and distance of candles from subjects must be consistent with efficacy data. Methods and sites described in the study protocol must be identical to the methods and sites stated on the product label. In these studies there were 1 or 2 candles placed 5 feet away from test subjects.

STUDY SUMMARIES

MRID 470191-01 *Release Rate of Linolool from Concealk Candles in Storage Conditions*

The release rate of linalool (grams of linalool/ hour, and average grams of linalool/ day) from unlit Conceal candles was measured over a time period of 2 years. The consisted of placing linalool candles in a warehouse at periodically record their weight, date and temperature over a period of 2 years. The amount of linalool released from the candles over time was measured as the difference in candle weight taken at time intervals for an elapsed period of 450 hours. The unlit candles were

measured with a Mettler Toledo Electronic Balance model # PB303-S having an accuracy of ± 0.001 . The measurements were repeated with candles 2 years old. The candles were stable for up to 2 years at ambient temperature, and the release rate of linalool remained consistent (approximately 0.0002 g/hr) over 2 years.

MRID 470191-02 *Linalool Candles as Spatial Repellents Against Natural Populations of Mosquitoes in Anahuac National Wildlife Refuge, Anahuac, Texas*

The study was conducted on concrete patios of a recreational vehicle park in the Anahuac Refuge, Texas Chenier Plain National Wildlife Refuge Complex, Chambers County, TX.

This location is a waterfowl, sub-tropical climate habitat to many mosquito species. The landing rate of mosquitoes on humans exceeded 5 mosquito landings per minute. The test was conducted at sunset during peak mosquito activity. The test was repeated on 6 nights (September 19 and 21, October 11 and 18, and November 18 and 19, 2006). There were 2 test stations, one with 1 linalool candle set up on each picnic table, and another with no candle as negative control. The candle was lit 30 minutes prior to initiation of the test. Four subjects (2 males and 2 females) sit down at 5 feet away from the table holding the candle. Wind direction was monitored so that there was no drift to the control station. The set up of control station was arrayed the same as the experimental station, but with no treatment. The same subjects rotated stations randomly for 3 trials each night. They used battery-operated aspirators to collect mosquitoes landing on their legs for an exposure period of 5 minutes. The collected mosquitoes were identified to species. Each night, 23 to 195 mosquitoes were collected and identified as *Eades vexans*, *Anopheles crucians*, *A. quadrimaculatus*, *Coquilletidia perturbans*, *Culex erraticus*, *C. quinquefasciatus*, *C. salianarius*, *Mansonia dyari*, *Ocherotatus taeniorhinchus*, *O. sollicitans*, and *Psorophora ciliata*. Data were transformed to percentage of each night total collection to adjust for daily differences in mosquito biting pressure. Treatment means were compared using ANOVA and t-test (Stat-ease, 2002). Mosquito landings were reduced by an average of 80% compared to control at a confidence level of 99%. The reported range in percent reduction was 69 to 92 percent.

MRID 470191-03 *Candles as Spatial Repellents Against Natural Populations of Mosquitoes in Arthur R. Marshall Loxahatchee National Wildlife Refuge, Boynton Beach, Florida.*

The study was conducted in ARM Loxahatchee NWR, Boynton Beach, Florida in March, 2004 (however, in Figures 1, 2, and 3, the data is reported as collected in 2006). This site is a sub-tropical climate with 221 square miles of wildlife protected habitat, inhabited by many species of mosquitoes. The landing rate counts at time of testing exceeded 5 landings per minute. The test was conducted at sunset at peak mosquito activity. The test consisted of 4 test stations, set up on the ground level on residential patios. Two linalool candles per station were placed at ground level, and subjects sat at a distance of 5 inches away from the lit candle. One station was kept without candle

as negative control. The test was repeated 8 nights from March 15 to 23, 2004. Four test subjects, 2 males and 2 females, participated in the study. An additional person timed landing counts on exposed forearm for one minute. All subjects rotate through all 4 stations at different times. At each station, subjects collected landing mosquitoes for 5 minutes using a battery-operated aspirator. Collected mosquitoes were identified to species. Each night, 18 to 195 mosquitoes were collected and identified as *Anopheles crucians*, *A. quadrimaculatus*, *Coquilletidia perturbans*, *Culex erraticus*, *C. nigripalpus*, and *mansonia dyari*. Data were transformed to percentage of each night total collection to adjust for daily differences in mosquito biting pressure. Treatment means were compared using ANOVA and t-test (Stat-ease, 2002). Mosquito landings were reduced by an average of 67% compared to control in test A, 68 % in test B, and 58 % in test C at a confidence level of 99%.

MRID 470191-04 *Field Evaluation of One Year Old 3.5% Linalool Candles Against Mosquitoes in Connecticut, USA*

The study was conducted on the front porch of 4 residences; two of the residences were in West Hartford, and the other 2 were in Windsor, CT. The test was repeated each night from July 1, 2, and 3 in West Hartford, and from August 1, 3, and 5, 2006, in Windsor, CT. Each night, the test was replicated 4 times. Two test stations were created each night. One station had no candles to be used as negative control. The second station had 2 candles, individually placed on 2 separate 30 inches tables. Both tables were 5 feet away from the test subjects. Two test subjects (1 female and 1 male) rotated randomly between stations so that each subject tested at each station twice for a total of 4 trials per night. During testing, subjects collected mosquitoes for 5 minutes using a battery-operated aspirator. Collected mosquitoes were identified to species. *Eades vexans*, *Anopheles punctipennis*, *A. quadrimaculatus*, *Coquilletidia perturbans*, *Culex salinarius*, *Ocherotatus japonicus*, *O. triseriatus*, *O. sticticus*, and *O. grossbecki*. Data from total collections were statistically analyzed using ANOVA and t-test (Stat-ease, 2002). Significance level for treatment means comparison was established at $P < 0.01$. Compared to control, mosquito landings were reduced 72.5 % in the presence of Conceal Candles.

BACKGROUND AND REVIEWER COMMENTS

Linalool has been reported to exhibit spatial repellency to mosquitoes in the published literature (Kline et al, 2003).

Study MRID 470191-04, *Field Evaluation of One Year Old 3.5% Linalool Candles Against Mosquitoes in Connecticut, USA*, is designed to evaluate the spatial repellency of linalool-based candles in the field. The study is inconclusive due to lack of information. The study report only includes a graph which shows that the total mosquitoes collected are below the >5 human landing rate counts stated on page 4. The numbers in that graph show a range of collected mosquitoes from less than 2 (maybe 1) to a number between 6 and 8 (maybe 7) for test station, and a range from 5 (approximately) to 16 total mosquitoes in the absence of the Conceal candle. Thus, as reported, this study is inconclusive.

Studies MRIDs 470191-03 and MRID 470191-02 are designed to assess efficacy of linalool-based candles in the field. The results reported from these studies show inconsistency in percentages of efficacy, and date of study performance. Calculated percentages show lower levels of efficacy than those reported in the studies. It is not clear how the investigator calculated the reported percentages of mosquito reduction due to the presence of the candle relative to control landings.

Cited Reference:

Kline DL, Bernier UR, Posey KH, Barnard DR. 2003. Olfactometric evaluation of spatial repellents for *Aedes aegypti*. J. Med. Entomol. 40(4): 463-467.